REMARKS

Claims 2-7, 18-20, and 22 are canceled without prejudice to applicants' right to claim the subject matter. Claims 1, 8 and 17 are currently amended. Claims 9-16, 23 read on non-elected subject matter and are identified as withdrawn.

Information Disclosure Statement

References identified by the Examiner as having incomplete citation or not submitted with the previously filed IDS are submitted in a supplemental IDS concurrently filed herewith.

Color Photographs

Applicants submit petition pursuant to 37 C.F.R §1.84(a)(2), three sets of color drawings and the appropriate fee set forth in 37 C.F.R §1.17(h).

This paper amends the specification to insert the language required as the first paragraph of the brief description of the drawings section.

Claim Objections

Currently amended claim 1 does not recite a "use" limitation. Claims 2-7, 18-20, and 22 are canceled without prejudice. Therefore, the Examiner's objection is moot.

Applicants respectfully note that claim 23 which recites a method for treatment of IBD is drawn to non-elected subject matter which has not been examined. Applicants request withdrawal of the objection that claim 23 is substantially duplicate of claim 8.

Claim Rejections Under 35 U.S.C. §112-First Paragraph

The Examiner alleges that claims 1-8 and 17-22 fail to comply with the enablement requirement.

Applicants traverse the rejection. In view of the Examiner's position that "intended use limitation does not distinguish the composition," currently amended claims do not recite

intended use as a claim limitation. Therefore, the claimed composition as recited in claims 1 and 17, and all dependent claims therefrom are not limited by a recited use.

MPEP 2164.01(c) states, *inter alia*, that: "In contrast, when a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for nonenablement based on how to use. If multiple uses for claimed compounds or compositions are disclosed in the application, then an enablement rejection must include an explanation, sufficiently supported by the evidence, why the specification fails to enable each disclosed use. In other words, if *any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention.* (emphasis added)"

As acknowledged by the Examiner (page 8 in the Office Action of August 31, 2006), the specification provides working examples for treating IBD with oxytocin and secretin. In addition to Example 7, which is referred to by the Examiner, Figures 19-27, and Examples 4, 5 also specifically describe effects of administration of a composition comprising oxytocin and secretin in an induced model of IBD, and a genetic model of IBD (IL-10 mutant mice). Therefore, the specification enables the use of the composition of oxytocin and secretin for the treatment of IBD. The specification also enables use of the claimed composition for treatment of IBS (see Example 4). Because the composition of oxytocin and secretin as claimed is not limited by a specific use, and the specification enables use of the claimed composition for the treatment of IBD, thereby not failing to enable *each* disclosed use, the specification is enabling for the claimed composition comprising oxytocin and secretin.

Specific factors, listed (1)-(9), as discussed by the Examiner on pages 5-9.

(1) The nature of the invention and (2) the breadth of the claims:

As discussed supra, the claimed composition is not limited by a recited use. Because the claimed composition is enabled for at least one use, i.e., the treatment of IBD, the claimed composition of oxytocin and secretin is enabled.

(3) The state of prior art and (4) the predictability or unpredictability of the art:

The Examiner cites a number of references as allegedly showing the unpredictability and/or lack of treatment of disorders such as CREST syndrome (The Mayo Clinic Internet Document), Progressive Systemic Sclerosis (Merck Manual 16th Edition (1992) R. Berkow, ed., pages 1321-1323), Autism (NIH News Alert-Internet Document "The Use of Secretin to Treat Autism," ABOUT.com-Internet Document "What drugs are used to treat autism?", C.R.Ellis et al.-Internet Document "Autism," Hollander et al. US Pub. 2006/0105939A1), IBS or IBD (IBS and IBD: "Two very different disorders"-Internet Document).

Applicants traverse the rejection. The references applied by the Examiner recite blanket generalizations that there are no treatments for the named disorders or that known treatments are few or ineffective. None of the references cited by the Examiner specifically teaches or suggests that a composition comprising a combination of oxytocin and secretin is not effective for the treatment of any of these conditions. Therefore, the cited references do not show that the claimed composition does not work for treatment of any of the named disorders. At most the references show that there is need for new treatments, a problem solved by the composition comprising oxytocin and secretin as claimed, and enabled in the instant specification.

The Examiner further alleges that IBS and IBD are different disorders with different symptoms, thereby involving different treatments. Applicants respectfully disagree. IBS is referred to as a functional disorder, which is typically diagnosed by a characteristic group of symptoms in the absence of detectable structural abnormalities. IBD is an inflammatory disorder which can also be characterized by various forms of chronic mucosal and/or transmural inflammation of the intestine. Although IBS does not usually produce the destructive inflammation found in IBD, recent evidence suggests mechanisms that might play a role in the pathophysiology of both disorders (See Bradesi et al., (2003) Inflammatory Bowel Disease and Irritable Bowel Syndrome: Separate or Unified? *Current Opinion in Gastroenterology* 19(4): 336-342). Therefore, therapeutic approaches which are effective in treatment if IBD can be effective in treatment of IBS.

(5) The relative skill of those in the art:

The Examiner alleges that the relative skill of those in the art is low with regards to: formulation of compositions having effective doses for the intended use recited, and in regards

to knowing *a priori* which compounds, e.g. protease inhibitors, will function in treating a condition they are not otherwise known to treat. Applicants traverse the rejections.

Paragraphs [0088] and [0089] describe therapeutic dose ranges which can be administered in treatments that use the claimed composition of secretin and oxytocin. Furthermore, paragraphs [0044], [0047], and [0222] recite specific doses of the claimed composition used in the Examples described in the specification.

Paragraph [0073] specifically describes that the protease inhibitors contemplated by the claimed invention are used in the composition to block or inhibit proteases. The ability of protease inhibitors to block proteases from degrading proteins or peptides is well known in the art. Therefore, the claimed composition of oxytocin and secretin and optionally with protease inhibitor is reasonably expected to have the activity of the oxytocin and secretin composition without protease inhibitor. The instant application has no claims directed to a protease inhibitor alone. Therefore, the specification need not enable a protease inhibitor for treatment of a condition previously unknown to be treated with protease inhibitors as required by the Examiner.

(6) The amount of direction or guidance and (7) the presence or absence of working examples, (8) The quantity of experimentation necessary:

As discussed supra, the specification fully enables use of the claimed composition comprising oxytocin and secretin, and optionally with a protease inhibitor for the treatment of IBD, and IBS.

The specification also specifically sets forth examples, *inter alia* in paragraph [0076], on how to administer the composition of oxytocin and secretin. Methods for administering peptide compositions are also well known in the art.

Example 3 of the specification, for example provides various assays, methods and test parameters that can be evaluated to determine the effect of maternal intervention on disorders with severe behavioral symptoms, such as conduct disorder, oppositional defiant disorder, reactive attachment disorder, attention deficit disorder, and attention deficit-hyperactivity

disorder. Paragraph [0163] specifically describes that "maternal intervention that includes reinstatement of specific components of maternal nurturing, . . . , and/or treatments that replicate these effects pharmacologically, can be effective in ameliorating severe behavioral symptomology." Paragraph [0198] further teaches that oxytocin and secretin are two neuropeptides involved in mother-infant behavior modulation. Methods of administering peptide compositions to subjects are taught by the specification and the specification provides guidance without undue experimentation on how to determine the effect of the claimed composition on disorders with severe behavioral symptoms. Therefore one of skill in the art would be able to carry out the claimed invention without undue expereimentation.

Claim Rejections Under 35 U.S.C. §103

The Examiner alleges that Claims 1-8 and 17-22 are unpatentable over Hollander (U.S. Pub. 2006/0105939) in view of NIH news alert ("The Use of Secretin to Treat Autism" Internet document dated 08/17/2001), and further in view of Swain (E. Swain, Pharmaeceutical and Medical Packaging (1999) and Pierce (Pierce Technical Resource Sheet TR0043.0 "Protein Stability and Storage" 6/03).

The Examiner alleges that Hollander teaches treating of autism with oxytocin, and discloses agents suitable for use in combination therapy as recited in paragraph [0046]. The Examiner further alleges that in view of *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980), it would have been obvious to combine oxytocin and secretin and make a composition for the treatment of autism, because oxytocin and secretin have been individually taught in the prior art as useful for treating autism. According to *In re Kerkhoven* "It is prima facie obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; idea of combining them flows logically from their having been individually taught in prior art; thus, claims that require no more than mixing together of two conventional spray-dried detergents set forth prima facie obvious subject matter."

Applicants respectfully traverse the rejection. Hollander teaches treatment of autism by administration of a therapeutic amount of oxytocin, or in combination therapy with any chemical compound. Agents and factors as recited by paragraphs [0039] and [0046] in Hollander, which

can be used in combination therapy include "sedatives, tranquilizers, antipsychotics, antidepressants, anticonvulsants, and the like. Agents may additionally include those capable of affecting the opiate, noradrenergic, dopaminergic, serotonergic, glutamatergic, and/or GABAergic systems. Agents may further affect gene transcription, specifically in genes responsible for brain development." Secretin is a peptide and one of ordinary skill in the art would not refer to secretin as a chemical compound. Because the combination therapy agents contemplated by Hollander are disclosed merely as categories of "agents and factors," Hollander does not each or suggest a specific peptide or hormone, let alone secretin, as an agent which can be used in combination with oxytocin. Therefore, Hollander fails to provide a specific motivation to combine two peptides or hormones to make a composition which comprises oxytocin and secretin as claimed. Because the alleged disclosure of a combination therapy as taught by Hollander does not teach or suggest combination of oxytocin and another peptide, let alone secretin, it would not have been obvious to one of ordinary skill in the art to use the teaching of Hollander in combination with the NIH alert which teaches secretin for the treatment of autism and make a composition which comprises oxytocin and secretin as claimed. Only with the benefit of hindsight would one look to Hollander and find motivation to combine oxytocin and secretin.

Furthermore, neither an alleged combination of oxytocin and secretin disclosed by Hollander in view of the NIH alert, nor an alleged combination of oxytocin and secretin according to the *prima facie* test of *In re Kerkhoven* teaches or suggests a combination of oxytocin and secretin that has a *synergistic effect*. In contrast, the claimed specific combination of oxytocin and secretin has a synergistic effect as described in the instant specification. Paragraphs [0075], [0086], and [0087] of the instant specification specifically refer to the synergistic therapeutic effect of the claimed combination of oxytocin and secretin. Also, results in Figure 22 show that a treatment with a combination of oxytocin and secretin leads to a better resolution of inflammatory infiltrates compared to a treatment with secretin alone. For example, paragraph [0047] which describes the results in Figure 22 specifically "[n]ote[s] the dramatic increase in inflammatory infiltrate in [Figure 22] (A) in the saline treated animal and [Figure 22] (B) in the Secretin (only) treated mouse and resolution of inflammation in [Figure 22] (C) after [Secretin/oxytocin] peptide treatment." Paragraph [0230] further states that "[t]here was a partial resolution of inflammation in the IL10-/- mouse after I.P. infusion of S[ecretin] and an

almost complete resolution of inflammation with combined S[ecretin]/OT[oxytocin] peptide therapy."

Although paragraph [0045] of Hollander contemplates delivery such that ". . . [an] agent and oxytocin or oxytocin analog would still be able to exert an advantageously combined (e.g. synergistic) effect . . . ," Hollander fails to provide a specific motivation to combine two hormones to make a composition which comprises oxytocin and secretin as claimed. As discussed supra, the references applied by the Examiner do not disclose or suggest the claimed combination of oxytocin and secretin. Therefore, the synergistic effect of the claimed combination is unexpected. Because the synergistic effect of the claimed composition of oxytocin and secretin is unexpected, the claimed composition is not rendered obvious by the references applied by the Examiner. *In re Wiechert*, 370 F.2d 927, 962, 152 USPQ 247 (CCPA 1967).

Applicants also traverse the Examiner's rejection that claims 1, 8, 17 and 21 are obvious over Hollander in view of the NIH news alert and further in view of Swain, which discloses packing of pharmaceuticals and Pierce, which discloses addition of protease inhibitors to protein solutions to lengthen shelf life.

In view of the foregoing arguments, the claimed combination of oxytocin and secretin is not obvious over Hollander in view of the NIH alert. Hollander in view of the NIH alert fails to render the claimed combination of oxytocin and secretin obvious because Hollander fails to provide specific motivation to combine oxytocin and secretin. Swain's disclosure of packaging pharmaceuticals does not cure the deficiency of Hollander in view of the NIH alert, and neither does Pierce, which discloses protease inhibitors, because neither Swain nor Pierce provide specific motivation to combine oxytocin and secretin. Therefore, Hollander in view of the NIH alert, and in further view of Pierce and Swain does not render the claimed composition obvious because neither Swain nor Pierce provide specific motivation to combine oxytocin and secretin to make the claimed composition. Furthermore, Swain and/or Pierce do not cure the deficiency of an alleged combination according to the test of *In re Kerkhoven* because neither Swain nor Pierce teach or suggest a combination of oxytocin and secretin which has a synergistic effect.

Thus, Hollander in view of the NIH alert combined further with Swain and Pierce does not render the claimed combination of secretin and oxytocin obvious.

Therefore, claim 8 which claims the pharmaceutical composition of claim 1 wherein the composition includes protease inhibitor(s), claim 17 which recites a kit comprising the combination of oxytocin and secretin, and claim 21 reciting the kit of claim 17 which includes protease inhibitor are not rendered obvious over of the combination of references applied by the Examiner. In view of the foregoing arguments, applicants respectfully request reconsideration and withdrawal of the rejections of claims 1, 8, 17 and 21.

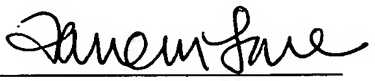
CONCLUSION

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Commissioner is authorized to charge any fees that might be due or credit any overpayment to Deposit Account No. 08-0219.

Respectfully submitted,

Dated: February 28, 2007



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